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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/912,609	07/25/2001	Evan C. Unger	UNGR-1599	8279

23980 7590 10/12/2006

MINTZ, LEVIN, COHN, FERRIS, GLOVSKY AND POPEO, P.C
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EXAMINER	
SOROUSH, LAYLA	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 10/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/912,609	UNGER ET AL.	
	Examiner	Art Unit	
	Layla Soroush	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8,9,12,14-16,20 and 40-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6, 8-9, 12, 14-16, 20, 40-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response filed June 26, 2006 presents remarks and arguments submitted to the office action mailed March 27, 2006 is acknowledged.

Applicant's amendments submitted June 26, 2006 is acknowledged wherein claims 1-6, 8-9, 14-16, 20, and 40-42 are amended.

Applicant's arguments over the 35 U.S.C. 103 (a) rejection of claims 1-6, 16, 20, and 40-42 over Gref US Patent 5,543,158 (Gref) in view of Quay EP 0727225 (Quay), Ruoslahti et al US Patent 5,981,478 (Ruoslahti), and Wallace US Patent 5,238,714 (Wallace) is not persuasive. Therefore, the rejection is maintained for reasons of record.

Applicant's arguments over the 35 U.S.C. 103 (a) rejection of claims 1-6, 8,9,12,14-16,20. and 40-42 over Hunter US Patent 6,759,431 (Hunter), in view of Domb et al US Patent 5,578,325 (Domb) and Ruoslahti is not persuasive. Therefore, the rejection is maintained for reasons of record.

The rejections are restated below for applicant's convenience.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6, 16, 20, 40-42 have rejected under 35 U.S.C. 103(a) as being unpatentable over Gref US Patent 5,543,158 (Gref) in view of Quay EP 0727225

(Quay), Ruoslahti et al US Patent 5,981,478 (Ruoslahti), and Wallace US Patent 5,238,714 (Wallace).

Gref discloses compositions comprising particles of a solid biodegradable core comprising PEG and PLGA loaded with a chemotherapeutic or immunosuppressive agent. (see col 3, lines 55-60; col 4, lines 45-65; col 12, lines 39-55; col 14, lines 25-65; claims 1-6). The internal solid core of Gref meets the limitations of the instant matrix. Gref states "a wide range of biological active materials or drugs can be incorporated into the polymer at the time of nanoparticle formation." (see col 12, lines 15-17). Gref then exemplified that hydrophobic drugs may be entrapped into the injectable particles (see col 12, lines 43-45). Gref further states that various types of therapeutic compounds may be incorporated or encapsulated within the internal biodegradable core. (see col 6, lines 1-15). Gref teaches that peptide fragments and/or antibodies can be covalently bounded to the outside of particles. (see col 5, lines 20-30; col 6, lines 26-31; col 18, lines 39-47). Such configuration meets the targeting element of the instant matrix system. Gref also teaches oral or injectable compositions that can be lyophilized which also fall within the scope of the instant matrix. (col 16, lines 30-45). Gref states that his particles may be attached to any particle specific ligand which can include peptides. (col 6, lines 18-25). Gref does not teach the instant targeting ligand CRDG or fu.

Quay, Ruoslathi and Wallace are used to show that polymeric microcapsules are readily attached to a targeting ligand to improve specific targeting to tissue cells of interest.

Quay teaches various ligands that can be conjugated to contrast agents in colloidal dispersions (abstract, page 3, lines 1-20). Such ligands include CAM ligands such as RGD or cyclic molecules including CRGD, which is specific integrins, and CAM ligands (page 7, line 20-page 8, line 62). The targeting ligands of Quay contain at least 2-10 amino acids.

Ruoslahti teaches specific targeting ligands such as CRGDC, and that they are more specific than RGD in inhibiting fibronectin attachment to alpha 5 – beta 1 (abstract; col 8, lines 21-67; col 9, lines 63-67).

Wallace teaches process of conjugating amino acid esters to the surface polymers of microcapsules to provide targeting to specific tissue cells (abstract). The polymeric microcapsules of Wallace can be made of PCL or polylactide (see col 1, lines 6-30; col 9, line 39-col 10, line 60).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to conjugate a specific targeting agent such as CRDGC of Ruoslahti to Grers microparticles to increase specificity of such particles toward a specific tissue cells by employing conjugation methods described by Quay and Wallace. One of ordinary skill in the art would have made such modifications of polymeric microparticles of Gref, because he would have had a reasonable expectation of success in enhancing cell specificity and thus enhancing intended therapeutic outcome.

Claims 1-6, 8-9, 12, 14-16, 20, 40-42 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Hunter US Patent 6,759,431 (Hunter), in view of Domb et al US Patent 5,578,325 (Domb) and Ruoslahti.

Hunter teaches various forms of polymeric drug delivery systems that may be used for delivery of camptothecin. (Abstract; col 15, line 20; col 74, lines 15-36). The polymeric moieties Of Hunter can be in various forms including drug-loaded microspheres or drug loaded polymeric pastes (col 29, line 50-col 31, line 20; col 56, line 50, col 58, line 67). The polymeric moieties of Hunter comprise PCL, PEG or copolymers thereof in the form of diblocks or paste (col 43, lines 10-col 44, lined 20; col 46, lines 5-65; col 56, lines 50-col 57, line 50; col 69, lines 15-65). Hunter explains that the type and concentration of his polymeric carrier can be fashioned to provide a desired release characteristic (col 21, line 46-co 22, line 65). Hunter also teaches targeted drug delivery to improve Hunter's teachings meets the limitations of claims 1-6, 8-9, 12-16. Hunter does not specifically teach the use of specific target peptides such as CRGDC to enhance the tissue specificity of its formulations.

Domb teaches that polymeric moieties of PCL or PEG diblock copolymers can be covalently attached to a targeting ligand to enhance their tissue specificity. (col 13, lines 1-15) (col 15, lines 25-line 65; col 21, lines 40-59).

Ruoslahti teaches specific targeting ligands such as CRGDC, and that they are more specific than RGD in inhibiting fibronectin attachment to alpha 5 -beta 1 (abstract; col 8, lines 21-67; col 9, lines 63-67).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to covalently attach a targeting ligand of choice, such as the CRGDC of Ruoslathi to the polymeric drug delivery systems of Hunter, because as elaborated in the art by Domb, one of ordinary skill in the art would have had a reasonable

expectation of success in improving the tissue specificity of Hunter's drug delivery system in modulating a5 -B1 receptor activity.

Response to Arguments

Applicant's arguments filed June 26, 2006 have been fully considered but they are not persuasive for the reasons set forth below.

With respect to the rejection of claims over Gref in view of Quay, Ruoslahti, and Wallace, Applicant argues that there the primary reference does not " a hydrophobic domain comprising a residue of an amino acid having a hydrophobicity value of at least 1.5 kcal/mol."

In response Examiner states that the Gref reference does teach the polymer comprising a hydrophobic block or blocks of the copolymer. Further the reference teaches hydrophobic compounds can be incorporated into the core of the injectable particles. Although, "hydrophilic fluorescent compounds can also be incorporated...the efficiency of encapsulation is smaller, because of the decreased compatibility of the hydrophobic core with the hydrophilic material. The hydrophilic material must be dissolved separately in water and a multiple emulsion technique used for fabrication of the particle." Hence, it would be obvious to one of ordinary skill in the art to incorporate a hydrophobic amino acid residue to insure compatibility of the hydrophobic core with the hydrophobic material.

Combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion can only establish obviousness, or motivation to do so found either in the references themselves or in the knowledge

generally available to one of ordinary skill in the art. See In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), and In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

Additionally, Applicant argues that the references fail to teach the polymer particles conjugated to peptides where "the peptide contains between 2 and 100 amino acid residues."

In this case, not only is there ample suggestion by the references to use a peptide containing between 2 and 100 amino acid residues but also there is ample knowledge generally available to one of ordinary skill in the art to reach the instantly claimed invention. Specifically, the targeting ligands of Quay contain at least 2-10 amino acids.

Moreover, to establish non-obviousness, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., 800 F.2d 1091,231 USPQ 375 (Fed. Cir. 1986). Here, the rejection is based on the combined teachings of the references not merely the teachings of Gref or Hunter.

For such reasons, the rejection is maintained.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Layla Soroush whose telephone number is (571)272-5008. The examiner can normally be reached on 8:30a.m.-5:00p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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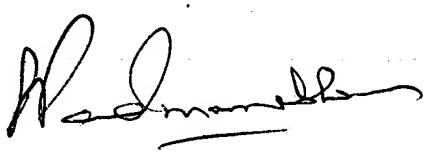

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